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# Comparison of Regular and Probiotic Yogurts in Treatment of Acute Watery Diarrhea in Children

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## Abstract

Diarrhea is among the leading causes of morbidity and mortality in children under five years of age, especially in developing countries. Due to dehydration and imbalance of water and electrolytes in the body. There is a need to introduce alternative ways for management of this common health problem. The aim of this study was to evaluate and compare the effects of regular and probiotic yogurt on duration and frequency of diarrhea in children aged one to five with acute watery diarrhea. Ninety patients were randomly assigned to three groups, two intervention groups, including regular and probiotic yogurt groups, and a control group. In the regular yogurt group, the first significant decrease in frequency of diarrhea was 2.15 ± 0.61 days and in the probiotic group was 2.65 ± 0.72 days after admission to the hospital.

**Keywords:** Probiotic; Regular; Yogurt; Diarrhea; Children

## Introduction

Diarrhea is defined as a condition in which watery stool is discharged from the bowel three or more times a day, indicating changes in quality and consistency of stool [1]. Another definition of diarrhea indicated that diarrhea is present when passage of watery stool is greater than 15 gm/kg/day in children younger than three and more than 200 gm/day in children older than three years of age. In general, diarrhea is not considered a disease but a set of symptoms that may be correlated with a variety of illnesses [2]. Diarrhea is a frequent symptom in children and is often relieved without serious complications and receiving medical interventions. In developed countries, diarrhea is considered a self-limited condition that does not require specific treatment [3]. However, in some cases, especially in developing countries, it may lead to serious complications, including severe malnutrition, morbidities, and even deaths, due to dehydration and imbalance of water and electrolytes in the body [3,4]. Due to the wide range of diarrheal signs and symptoms, it is important to detect and treat the patients, especially pediatric patients, who require further interventions for preventing serious complications [1].

Types of diarrhea based on duration of the symptoms include acute, chronic, and persistent diarrhea. The acute diarrhea is mostly caused by viruses and lasts less than two weeks [3]. Rotavirus-associated diarrhea accounts for about 760,000 annual deaths and 40% of hospitalizations in children under five years of age across the world [5]. Persistent diarrhea, lasting two to four weeks, and chronic diarrhea, lasting longer than four weeks, may be due to different gastrointestinal disorders, such as infections, inflammatory bowel diseases, and irritable bowel syndrome [1]. Because of the highest rate of acute diarrhea as compared to other types of diarrhea as well as other diseases, acute diarrhea is one of the leading causes of morbidity and mortality in children around the world [3].

The high morbidity and mortality rates of acute diarrhea urged the World Health Organization [6] to set out an aggressive research agenda regarding management of diarrhea with an emphasis on innovative prevention and control strategies in developing countries. The WHO addressed the strategies that may lead to improving sanitation and access to clean drinking water and proper nutrition. Researchers have also reported that early oral rehydration and nutrition have been shown to be the main interventions in management of diarrhea [6]. For example, oral rehydration therapy/solution (ORS), the most common approach for management of diarrhea, prevents about three million dehydration-related deaths in a year [7]. Recently, the most important goal in management of acute diarrhea is rehydration therapy to correct fluid, glucose, and electrolyte deficits in the body [8]. However, rehydration therapy is not effective for management of the severity and duration of acute diarrhea [8]. Due to the likelihood of serious complications associated with prolonged and acute dehydration in children under five years old, there is a need to investigate further interventions to introduce innovative approaches to reduce duration and frequency of diarrhea as well as liquid and electrolyte losses within the first week of incidence [9].

Complementary and alternative medicine is a set of unconventional medical interventions including the use of biologically-based products such as dietary supplements and exercises [10,11]. Probiotics, as biologically-based products, have been shown to be effective for reducing duration of diarrhea and accelerating recovery from acute diarrhea [12]. Probiotics are small, single-celled organisms or bacteria. Similar to the gastrointestinal tract's beneficial microorganisms, probiotics are non-pathogenic microorganisms that are essential for tract development and function. Probiotics may settle and colonize in the intestine and adjust the microflora and metabolic activities in the intestine, resulting in positive outcomes for human hosts. Positive outcome suggest tailored probiotics for the treatment of acute diarrhea [12]. Probiotics can benefit the host and act against gastrointestinal pathogens via a variety of mechanisms and activities, including the production of antimicrobial

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and toxic agents; competition with pathogens for colonization sites and nutrients; alteration of the intestinal environment through different methods, such as synthesizing vitamin B; and reinforcement of the host's defense system [13,14]. Vandenplas reported that probiotics are also effective for reducing symptoms of irritable bowel syndrome and inflammatory bowel diseases, such as Crohn's disease [15].

In addition to the research on probiotics in the management of diarrhea, it has been shown that yogurt that lacks probiotics-regular yogurt-can also be effective in reducing the duration of diarrheal episodes [16]. Capurso; Binnendijk and Rijkers have reported similar and positive effects of yogurt and probiotics in improving several outcomes related to the treatment of diarrhea, such as duration, frequency, and severity of diarrhea as well as hospital stay and weight loss [17,18].

Researchers have also endeavored to investigate the effectiveness of probiotic yogurt on the management of diarrhea; however, their results have still remained inconclusive, and there are debates regarding the use of probiotics, including probiotic yogurt, for the management of diarrhea. Francavilla et al. stated that there is no indication for effectiveness of probiotics in the management of diarrhea in children [19]. However, reinforcing findings on the effectiveness of probiotics, Agustina et al. and Narayan et al. found that probiotic bacteria and dairy products have a considerable association in the management of diarrhea. In the studies that indicated the effectiveness of probiotics, it is reported that dairy products, such as milk and yogurt, may provide a desirable environment for delivery of probiotics in the body [20,21]. Dairy products can protect the probiotic bacteria and increase their chance of survival through the gastrointestinal tract into the intestine [22]. Conway et al. investigated the effects of regular yogurt and probiotic yogurt on diarrheal patients and reported that both types of yogurt had significant effects for reducing duration of acute diarrhea [23]. Perez and Canani also indicated that whereas probiotics may have shown valuable effects on diarrheal patients, they require further examinations [24,25]. The inconclusive effectiveness of probiotic yogurt according to the literature calls for further clinical trials for verification of the previous findings.

Children of developing countries consistently experience the complications associated with diarrheal diseases, including malnutrition, delayed physical development, and early childhood mortality that require accurate and timely interventions, which are considerably understudied [26]. In Iran, it is estimated that diarrhea is the fourth cause of annual deaths in children under five years of age [27]. Since the irreversible complications of childhood diarrhea are mostly frequent in low-income households and probiotic yogurt is more expensive than regular yogurt, it is also valuable to compare the effects of these two types of yogurt to address the cost-effective management of the disease, especially in low-income populations who have the highest diarrheal morbidity and mortality rates [27,28]. To our knowledge, this is the first study that investigates and compares the effects of regular and probiotic yogurts for the management of diarrhea among children in Iran. The purpose of this study was to evaluate and compare the effects of regular and probiotic yogurts on duration and frequency of acute watery diarrhea in children aged one to five with acute watery diarrhea in Iran. Children under the age of five have the highest rates of incidence and complications of acute diarrhea. However, compared to children younger than one year of age, children aged from one to five have lower food and nutrition restrictions [29].

### Ethics statement

The Ethics Committee of Kashan University of Medical Sciences approved the study design. Written consent forms were signed by parents before the study.

## Methods

### Design and data collection

A double-blind clinical trial was performed on 90 pediatric patients with acute diarrhea who had been referred to an outpatient clinic and then hospitalized in the university research hospital of Shahid Beheshti Hospital in Kashan, Iran from May 2013 to July 2014. Inclusion criteria included hospitalized patients (who were hospitalized after referral from the outpatient clinic) aged one to five years old with acute, non-bloody, non-bacterial diarrhea for less than 48 hours and moderate dehydration. The exclusion criteria were severe dehydration, medication and/or antibiotic consumption, severe vomiting, different nutritional diet, convulsion, laboratory detection of inflammatory cells in stool samples, and clinical or laboratory signs of any type of coexisting diseases. The nutritional diet for patients was identified by the ward's nutritionist daily; thus, any patient receiving a different diet from other patients in the study was excluded. Patients with severe dehydration were excluded from this study because these patients required an additional intervention of intravenous fluids. Children with no dehydration were also excluded as they did not require hospitalization. The degree of dehydration and vomiting was assessed on the basis of the guidelines identified by the WHO [6]. All of the patients were accompanied by their mothers in the pediatric ward.

The study sample size was determined using the Pocock's formula and the following assumptions: power=0.80, $\alpha$=0.05, $\beta$=0.20, the minimum expected difference in standard deviation=3.6, and the minimum expected difference in means=2.40 [30]. The sample size in each group was estimated to be 30 participants. Among 134 children with diarrhea who were initially evaluated in terms of eligibility for inclusion in the study, 90 patients had the inclusion criteria and their mothers' consent to participate.

The first or second author/investigator, two pediatric specialists, evaluated all the diarrheal children in the outpatient clinic regarding the criteria for inclusion in the study. One of these authors visited the participants on every shift of the day. Additionally, the first author visited all the participants every day once in a day. For the purpose of generation of randomization, we used a numerical table that utilized numbers, 1-90, in which each number was specified to be assigned to one of three groups, participants using a simple randomization technique. Children who met the criteria for the study were allotted a number by the investigators at the time of admission. Intervention was performed in collaboration with the pediatric ward staff nurses. The staff nurses were trained about the use of the randomization table and delivery of the yogurts to the patients in the intervention groups. Using the table, the staff nurses assigned the children to three groups: Two intervention groups, including regular yogurt and probiotic yogurt groups, and a control group. The investigators were not informed of the assignments.

Demographic questionnaires that consisted of questions about patients' age and gender and their mothers' educational status were completed by parents at the beginning of the study. Additionally, at the time of admission to the hospital, a thorough medical history was obtained and recorded by the first or second investigator. This medical history addressed the history of the current episode of diarrhea,

including duration and frequency, current and past medications and medical disorders, and a physical examination to confirm the meeting of the criteria for the study.

### Procedure

As a part of standard care for hospitalized diarrheal children, all patients were provided with low osmolality ORS (ORS-224; marketed by CURATUO Health Care Pvt. Ltd.) by hospital staff. The low osmolality ORS has a total osmolality of 224 mmol/liter, and its ingredients include 84 mmol/liter glucose, 60 mmol/liter sodium, 10 mmol/liter citrate, 20 mmol/liter potassium, and 50 mmol/liter chloride. Over the course of treatment in the hospital, the amount of ORS for all the participants was 75 ml/kg every four to six hours, based on the children's sleep time. This amount was followed by a maintenance amount of 10-20 ml/kg for each passage of stool. The daily nutritional diet was identified by the pediatric ward's nutritionist. Based on the inclusion/exclusion criteria, the diet was the same for all the participants.

The participants in the control group received the nutritional diet as well as the low osmolality ORS. In addition to the diet and the low osmolality ORS, the regular yogurt group received 15 mg/kg of regular yogurt each four to six hours over five days. In addition to the nutritional diet and the low osmolality ORS, the probiotic yogurt group participants received 15 mg/kg of market available probiotic yogurt (Manufactured in Iran by Pegah Golpayegan) each four to six hours over five days. If the patients vomited after receiving the yogurt and/or ORS, the patients would receive the ORS and/or yogurt again. All the patients were routinely visited daily by a single physician (the first author) until discharge. Passage of formed stool and no stool passage for 12 consecutive hours were the criteria for discharge. The participants were discharged after 24 hours of meeting these criteria.

For the purpose of this study and to accurately evaluate the frequency and duration of diarrhea, the patients were also visited in each shift by the first or second authors, and the frequencies of diarrheal episodes were documented in charts provided for the study. The frequencies of the diarrhea episodes were also routinely documented by resident pediatric physicians in patients' charts. To ensure the validity of these documents, the authors verified the documented frequencies via comparing the two charts.

For the purpose of this study, the duration of diarrhea was measured at three points of time. Duration was referred to as the number of days at the three specific points of time minus one. The first duration of diarrhea was calculated at the beginning of the study (at the time of admission to the pediatric ward), the second duration was measured in the interim of the study (at the time of significant decrease in the frequency of diarrhea), and the third duration was measured at the end of the study (at the time of complete recovery from diarrhea/24 hours before discharge). At the beginning of the study, the first duration was considered the number of days from the incidence of diarrhea to the time of admission. The second duration refers to the number of days from admission to first observed significant decrease of frequency of diarrhea. At the end of the study, the third duration was defined as the number of days from admission to complete recovery of patients. The patients were discharged 24 hours after cessation of diarrhea; therefore, the duration at the end of the study was equal to the number of days of hospital stay minus one. Frequency was defined as the number of bowel passages during a day. Frequency was measured daily until discharge.

Data were analyzed using SPSS version 16. The repeated measure ANOVA was used to compare the groups across the three times. The chi-square test was used to examine differences among the groups. Statistical significance was set at 0.05.

## Results

The mean age of patients in the traditional yogurt group was 31.77 ± 7.70 months, in the probiotic yogurt group was 32.83 ± 9.09 months, and in the control group was 30.90 ± 8.08 months. From the total of 90 patients, 50% in the regular yogurt group, 56.7% in the probiotic yogurt group, and 60% in the control group were male. No significant differences were observed between the three groups regarding their characteristics, including age, gender, and mothers' education ($p>0.05$) (Table 1). At the beginning of the study, the three groups were not also different in terms of the duration (first duration) and frequency of diarrhea (Table 2).

Differences in the durations and frequency of diarrhea among the three groups were significant across the course of the study and interventions (Table 2). The mean scores of the second duration were significantly higher in the control group (3.28 ± 0.89 days) compared to the regular (2.82 ± 0.51 days) and probiotic (2.65 ± 0.72 days) yogurt groups. The mean scores of the third duration in the control group (4.25 ± 1.27 days) were also greater than the regular (3.56 ± 0.94 days) and probiotic (3.37 ± 0.83 days) yogurt groups. The differences in the second duration ($F=2.36$, $p=0.01$) and third duration ($F=3.32$, $p=0.02$) were significant between the intervention groups and the control group.

On the second day after admission, the differences between the frequency of bowel passage between the three groups were again not significant. On the third day after admission, the frequency of bowel passage was normal in the regular (2.15 ± 0.61) and probiotic (2.01 ± 0.37) yogurt groups; however, in the control group, the frequency of bowel passage (7.18 ± 2.13) indicated the continuation of diarrheal episodes. On the same day, the differences between the intervention groups, regular and probiotic yogurt groups, and the control group were significant ($F=2.32$, $p=0.03$). The results of the post-hoc LSD test did not indicate any significant difference between the regular and probiotic groups in terms of their duration and frequency of diarrhea over the course of the study.

## Discussion

In the current study, we found that regular and probiotic yogurts can be effective for the management of diarrhea. All the participants recovered from diarrhea within a maximum of six days and were discharged 24 hours after their recovery or cessation of diarrhea. The findings showed that over the course of the treatment, the duration and frequency of diarrhea decreased faster in the regular and probiotic yogurt groups as compared to the control group. Comparing the three groups, the intervention groups' lower time intervals from admission to the initial significant decrease of the frequency (the second duration) as well as complete recovery (the third duration) can indicate the effectiveness of probiotic and regular yogurt in the management of diarrhea. Our results did not represent any significant difference between the regular and probiotic groups' recovery process. Although our initial focus was not on hospital stay duration, the results of our study indicated the influence of regular and probiotic yogurts on reducing the hospital stay in our participants.

Research has progressively indicated the importance of innovative and alternative medicine for improving general health, reducing symptoms, and decreasing negative consequences of diseases and

| Variable | | Regular yogurt group | Probiotic yogurt group | Control group | *p* value |
|---|---|---|---|---|---|
| Age (month) Mean ± SD | | 31.77 ± 7.70 | 32.83 ± 9.09 | 30.90 ± 8.08 | 0.66 |
| Gender (*n* %) | Female | 15 (50%) | 13 (43.3%) | 12 (40%) | 0.73 |
| | Male | 15 (50%) | 17 (56.7%) | 18 (60%) | |
| Mothers' educational status (*n* %) | Less than HS diploma | 5 (16.6) | 8 (26.6) | 10 (33.3) | 0.81 |
| | Received HS diploma | 12 (40) | 10 (33.4) | 13 (43.4) | |
| | College degree | 13 (43.4) | 12 (40) | 7 (23.3) | |

**Table 1:** Patients' demographic characteristics.

| Variable | | Regular yogurt group (Mean ± SD) | Probiotic yogurt group (Mean ± SD) | Control group (Mean ± SD) | ANOVA |
|---|---|---|---|---|---|
| Frequency | First day | 7.9 ± 3.7 | 7. 7 ± 2.2 | 8.1 ± 3.2 | F=4.18 *p*=0.22 |
| | Second day | 7.64 ± 2.3 | 7.34 ± 3.18 | 7.73 ± 2.94 | F=4.38 *p*=0.29 |
| | Third day | 2.15 ± 0.61 | 2.01 ± 0.37 | 7.18 ± 2.13 | F=2.32 *p*=0.03 |
| | Fourth day | 1.86 ± 0.82 | 2.13 ± 0.27 | 3.98 ± 1.12 | F=2.22 *p*=0.02 |
| | Fifth day | - | - | 1.74 ± 0.67 | |
| Repeated measure ANOVA** | | *F*=4.65 *p*=0.01 | *F*=3.65 *p*=0.02 | *F*=2.35 *p*=0.06 | |
| Duration (Day) | First duration | 1.17 ± 0.38 | 1.33 ± 0.55 | 1.22 ± 0.48 | F=1.26 *p*=0.14 |
| | Second duration** | 2.82 ± 0.51 | 2.65 ± 0.72 | 3.28 ± 0.89 | F=2.36 *p*=0.01 |
| | Third duration | 3.56 ± 0.94 | 3.37 ± 0.83 | 4.25 ± 1.27 | F=3.32 *p*=0.02 |

*Duration refers to as the number of days at the three specific points of time minus one.
**Using the post-hoc test after repeated measure ANOVA, the second duration was identified. The second duration is the number of days from admission to first observed significant decrease of frequency of diarrhea minus one.

**Table 2:** Frequency and duration* of diarrhea in the three groups.

diseases' conventional treatments [31-33]. Due to the overwhelming rates of diarrhea and its complications in children, researchers have also endeavored to find alternative ways to reduce the duration of recovery from diarrhea. Recently, researchers have supported the importance of microorganisms in the management of diarrhea and reported that some microorganisms or bacteria, such as probiotics, may help treatment and prevention of diarrhea [34]. In this regard, Dinleyici et al., Florez et al. and Canani et al. in their studies assessed the effects of probiotics on clinical outcomes of children with infectious diarrhea [25,35,36]. They reported the significant effects of probiotics on the clinical outcomes of diarrhea, such as duration and frequency. Recruiting children with acute rotavirus-associated diarrhea, Ahmadi et al. [34] verified the results of Canani et al. [25] regarding the effectiveness of probiotics in the management of diarrhea.

Furthermore, the use of regular yogurt in diarrheal disorders has a traditional history among people across many countries. Several research teams investigated the effects of regular yogurt and reported its positive effects on the management of diarrhea [37,38]. Pashapour and Iou found that regular yogurt was effective in improving the clinical outcomes of infants with diarrhea in terms of their hospital stay duration, frequency of diarrhea, and weight loss [37]. Our findings verified the results of these studies as well as the study conducted by Choudhary et al. on the effects of regular and probiotic yogurts in the treatment of acute childhood diarrhea [39]. Choudhary et al. reported that both types of yogurt were effective in decreasing the disorder's duration and frequency [39]. Heydarian et al. also studied the effects of the two types of yogurt and reported that probiotic yoghurt was effective in the management of acute diarrhea; however, their results regarding regular yogurt were not significant [30]. Despite the contradictory findings of Heydarian et al.'s study, results from the other relevant studies were in agreement with each other as well as with our study in terms of the effectiveness of regular yogurt in the management of acute childhood diarrhea. Nevertheless, the findings of clinical trials on probiotics, including probiotic yogurt, have considerably remained controversial and inconclusive regarding the effectiveness of these products in the management and clinical outcomes of diarrhea [40,41]. These inconsistent results might be due to differences in studies' populations, the types of diarrhea, the amounts of the provided probiotics, and other methodological considerations, such as participants' criteria for inclusion in the studies.

The present study showed that the administration of probiotic and regular yogurts to children with acute diarrhea can decrease the duration and frequency of diarrhea as well as their hospital stay. Therefore, these results can be integrated with the results of the studies that indicated the effectiveness of these products for ultimate application in evidence-based practice. Furthermore, since our results did not indicate any difference between the regular and probiotic yogurts, we also can recommend the use of regular yogurt, as the more

accessible and affordable dairy product in developing countries, for the management of diarrhea. However, because the consumption of both types of yogurt decreased the patients' hospital stay, both interventions can also be considered as cost-effective approaches to the management of diarrhea.

Generalizability of our findings is limited by the small sample size and lack of data on the participants' etiology of diarrhea. There was no technique for distinguishing the etiology of acute diarrhea, such as involvement of rotaviruses, in our participants. There was no control over the patients' daily nutritional diet by the investigators. However, the patients with the same scheduled diet were included in this study. We recommend further relevant clinical trials on children with different ages to provide rigorous evidence for improving practice.

## Conclusions

The probiotic and regular yogurts had positive effects on the management of childhood acute diarrhea in our study. Diarrheal disorders leave complications mostly in economically disadvantaged populations. Based on our findings, we can conclude that regular yogurt may have the same advantages in the treatment of diarrhea as probiotic yogurt, which may imply the cost-effectiveness and acceptability of the regular yogurt for treatment of this common health problem for all affected patients. However, reducing the hospital stay is another rationale that can justify the cost-effectiveness of both products in the recovery process of childhood diarrhea, especially in developing countries.

### References

1. DuPont HL (2016) Persistent Diarrhea: A Clinical Review. JAMA 315: 2712-2723.
2. Pereg D, Kimhi O, Tirosh A, Orr N, Kayouf R, et al. (2005) The effect of fermented yogurt on the prevention of diarrhea in a healthy adult population. Am J Infect Control 33: 122-125.
3. Keusch GT, Walker CF, Das JK, Horton S, Habte D (2016) Diarrheal Diseases. In: Black RE, Laxminarayan R, Temmerman M, Walker N (eds.). Disease Control Priorities, 3rd edn. Reproductive, Maternal, Newborn and Child Health: Washington (DC): The International Bank for Reconstruction and Development/ The World Bank.
4. Senbanjo IO, Ch'ng CL, Allen SJ (2016) Improving the management of acute diarrhoea and dehydration in under-5 children in a paediatric referral facility in Lagos, Nigeria. Paediatr Int Child Health, pp: 1-6.
5. Gonzales SC, Bada MC, Rojas GR, Bernaola AG, Chavez BC (2012) Clinical practice guideline on the diagnosis and treatment of pediatric acute infectious diarrhea in Peru - 2011. Revista de Gastroenterologia del Peru: Organo Oficial de la Sociedad de Gastroenterologia del Peru 32: 100-105.
6. World Health Organization (2010) WHO Recommendations on the Management of Diarrhoea and Pneumonia in HIV-Infected Infants and Children: Integrated Management of Childhood Illness (IMCI).
7. Tian L, Zhu X, Chen Z, Liu W, Li S, et al. (2016) Characteristics of bacterial pathogens associated with acute diarrhea in children under 5 years of age: a hospital-based cross-sectional study. BMC Infectious Diseases 16: 253.
8. Black RE, Levin C, Walker N, Chou D, Liu L, et al. (2016) Reproductive, maternal, newborn and child health: key messages from Disease Control Priorities. 3rd edn. Lancet 388: 2811-2824.
9. Abegaz TM, Belachew SA, Abebe TB, Gebresilassie BM, Teni FS, et al. (2016) Management of children's acute diarrhea by community pharmacies in five towns of Ethiopia: simulated client case study. Ther Clin Risk Manag 12: 515-526.
10. Duncan HJ, Pittman S, Govil A, Sorn L, Bissler G, et al. (2007) Alternative medicine use in dialysis patients: potential for good and bad. Nephron Clin Pract 105: 108-113.
11. Nowack R, Ballé C, Birnkammer F, Koch W, Sessler R, et al. (2009) Complementary and alternative medications consumed by renal patients in southern Germany. J Ren Nutr 19: 211-219.
12. Lau CS, Chamberlain RS (2016) Probiotics are effective at preventing Clostridium difficile-associated diarrhea: a systematic review and meta-analysis. International Journal of General Medicine 9: 27-37.
13. Kalima K, Lehtoranta L, He L, Pitkaniemi J, Lundell R, et al. (2016) Probiotics and respiratory and gastrointestinal tract infections in Finnish military conscripts - a randomized placebo-controlled double-blinded study. Beneficial microbes 7: 463-471.
14. Islam SU (2016) Clinical Uses of Probiotics. Medicine 95: e2658.
15. Vandenplas Y (2016) Probiotics and prebiotics in infectious gastroenteritis. Best Pract Res Clin Gastroenterol 30: 49-53.
16. Rijkers GT, de Vos WM, Brummer RJ, Morelli L, Corthier G, et al. (2011) Health benefits and health claims of probiotics: bridging science and marketing. Br J Nutr 106: 1291-1296.
17. Capurso L (2016) Probiotics. Recenti Prog Med 107: 267-277.
18. Binnendijk KH, Rijkers GT (2013) What is a health benefit? An evaluation of EFSA opinions on health benefits with reference to probiotics. Benef Microbes 4: 223-230.
19. Francavilla R, Cristofori F, Indrio F (2016) Indications and Recommendations by Societies and Institutions for the Use of Probiotics and Prebiotics in Paediatric Functional Intestinal Disorders. J Pediatr Gastroenterol Nutr 63: 36-37.
20. Agustina R, Kok FJ, van de Rest O, Fahmida U, Firmansyah A, et al. (2012) Randomized trial of probiotics and calcium on diarrhea and respiratory tract infections in Indonesian children. Pediatrics 129: 1155-1164.
21. Narayan SS, Jalgaonkar S, Shahani S, Kulkarni VN (2010) Probiotics: current trends in the treatment of diarrhoea. Hong Kong Med J 16: 213-218.
22. Fox MJ, Ahuja KD, Robertson IK, Ball MJ, Eri RD (2015) Can probiotic yogurt prevent diarrhoea in children on antibiotics? A double-blind, randomised, placebo-controlled study. BMJ Open 5: e006474.
23. Conway S, Hart A, Clark A, Harvey I (2007) Does eating yogurt prevent antibiotic-associated diarrhoea? A placebo-controlled randomised controlled trial in general practice. Br J Gen Pract 57: 953-959.
24. Perez C (2015) Probiotics for the treating acute diarrhea and preventing antibiotic-associated diarrhea in children. Nutr Hosp 31: 64-67.
25. Canani RB, Cirillo P, Terrin G, Cesarano L, Spagnuolo MI, et al. (2007) Probiotics for treatment of acute diarrhoea in children: randomised clinical trial of five different preparations. BMJ 335: 340.
26. Agarwal KN, Bhasin SK (2002) Feasibility studies to control acute diarrhoea in children by feeding fermented milk preparations Actimel and Indian Dahi. European journal of clinical nutrition 56: S56-59.
27. Ghasemi A, Talebian A, Masoudi Alavi N, Mousavi GH (2013) Knowledge of Mothers in Management of Diarrhea in Under-Five Children, in Kashan, Iran. Nursing and Midwifery Studies 1: 158-162.
28. Saberi F, Amini S, Jan Nesari R (2014) Mothers' roles in prevention and care of diarrhea in children of aran and bidgol, Iran. Nurs Midwifery Stud 3: e19985.
29. Fuessl HS (2015) Yogurt to control antibiotic-induced diarrhea in children? MMW Fortschritte der Medizin 157: 37.
30. Heydarian F, Kianifar HR, Ahanchian H, Khakshure A, Seyedi J, et al. (2010) A comparison between traditional yogurt and probiotic yogurt in non-inflammatory acute gastroenteritis. Saudi medical journal 31: 280-283.
31. Ajorpaz NM, Shahshahani MS, Rahemi Z (2013) The effect of pure and impure honey on nausea, vomiting and headache of dysmenorrhea. Journal of Kermanshah University of Medical Sciences 16: 510-517.
32. Rahimimoghadam Z, Rahemi Z, Mirbagher AN, Sadat Z (2016) Effects of Pilates exercise on general health of hemodialysis patients. Journal of Bodywork and Movement Therapies 21: 86-91.
33. Eshgh ZM, Rahemi Z, Alavi MH, Hoviattalab SK, Yaghamaei F (2011) Effects of walking on quality of life of mastectomy patients at selected hospitals of Tehran. Iran J Nurs Midwifery Res 16: 299-303.
34. Ahmadi E, Alizadeh-Navaei R, Rezai MS (2015) Efficacy of probiotic use in acute rotavirus diarrhea in children: A systematic review and meta-analysis. Caspian J Intern Med 6: 187-195.
35. Dinleyici EC, Vandenplas Y (2015) Lactobacillus reuteri DSM 17938 effectively reduces the duration of acute diarrhoea in hospitalised children. Acta Paediatrica 103: 300-305.

36. Florez ID, Al-Khalifah R, Sierra JM, Granados CM, Yepes-Nunez JJ, et al. (2016) The effectiveness and safety of treatments used for acute diarrhea and acute gastroenteritis in children: protocol for a systematic review and network meta-analysis. Systematic Reviews 5: 14.

37. Pashapour N, Iou SG (2006) Evaluation of yogurt effect on acute diarrhea in 6-24-month-old hospitalized infants. The Turkish Journal of Paediatrics 48: 115-118.

38. El-Soud NH, Said RN, Mosallam DS, Barakat NA, Sabry MA (2015) Bifidobacterium lactis in Treatment of Children with acute Diarrhea. A Randomized Double Blind Controlled Trial. Open Access Maced J Med Sci 3: 403-407.

39. Choudhary M, Sharma D, Beniwal M, Dabi D, Pandita A (2015) Traditional Yoghurt and Probiotic in Treatment of Acute Childhood Diarrhoea: A Blinded Randomized Controlled Non - Inferiority Trial. J Pediatr Neonatal Care 2: 58.

40. Sipsas NV, Zonios DI, Kordossis T (2002) Safety of Lactobacillus strains used as probiotic agents. Clinical Infectious Diseases 34: 1283-1284.

41. Htwe K, Yee KS, Tin M, Vandenplas Y (2008) Effect of Saccharomyces boulardii in the treatment of acute watery diarrhea in Myanmar children: a randomized controlled study. The American Journal of Tropical Medicine and Hygiene 78: 214-216.